Some factors that could increase the rate of medication errors

- More rapid throughput of patients
- New drug developments, extending medicines into new areas
- Increasing complexity of medical care
- Increased specialisation
- Increased use of medicines generally
- Sicker and older patients, more vulnerable to adverse effects

tions might be in preventing the most serious errors (most studies have identified potential errors, rather than harm), nor how much they would cost—astonishing for an organisation whose primary function is to ensure that public funds are well spent.

A concern mentioned only briefly in the report is that current undergraduate medical courses "do not provide a thorough knowledge of safe medicines prescribing and administration" for junior doctors. As well as improving systems to avoid prescribing errors, there is a pressing need to improve the training of prescribers at all levels.

Tomorrow's Doctors from the General Medical Council[6] emphasised closer integration between subjects, reduced factual burden, greater student choice, and problem based learning. This has changed undergraduate education for the better in many ways but has marginalised individual disciplines, even disciplines like clinical pharmacology and therapeutics that teach skills that all doctors require. Although the council identified the principles of therapy as a key component of any undergraduate core curriculum,[6] few courses ensure that undergraduates are taught and tested on how to prescribe and give drugs safely. A firm grounding in the principles of therapeutics is essential in undergraduate education, so that tomorrow's doctors know how to weigh up the potential benefits and hazards of treatment, monitor drug effects, understand the reasons for variability in drug response, base prescribing choices on sound evidence, and keep up to date in the future.[7]

Assessment drives and consolidates learning: although examination in individual disciplines is now discouraged, prescribing and administering drugs–which are central to almost all medical care—are different. Together they are essential skills for the newly qualified doctor. Proficiency could be demonstrated in many ways,[8] for instance as part of an objective structured clinical examination, but students should not be able to compensate for a poor performance in this high risk clinical activity by good performances in other areas.

Undergraduate education has to be supported by induction programmes for junior doctors that can address specific issues in each hospital and by continuing education programmes. But these can be effective only if they build on a firm foundation. We have described here education of medical students, but the same issues apply to other professions as they acquire prescribing rights within the NHS. Current programmes for training nurse prescribers (25 days of theory, and two months' supervised prescribing practice) might be looked at enviously in many medical schools.

A report from the United States about medication errors suggests strongly that identifying competency in this key area of patient safety should be the responsibility of the professional licensing body.[3] The General Medical Council is currently in consultation about a revised version of *Tomorrow's Doctors*. We hope that it will respond to these concerns by providing clear directions to the United Kingdom's medical schools about the need for the learning and assessment of the skills needed to use drugs safely, effectively, and cost effectively. The Audit Commission is right to worry about medication errors, but preventing them is likely to be difficult and should not concentrate on pharmacists or computers to the exclusion of those who prescribe and give drugs.

Simon Maxwell *senior lecturer*

Clinical Pharmacology Unit, University of Edinburgh, Western General Hospital, Edinburgh EH4 2XU

Tom Walley *professor*

Department of Pharmacology and Therapeutics, University of Liverpool, Liverpool L69 3GF

Robin E Ferner *director*

West Midlands Centre for Adverse Drug Reaction Reporting, City Hospital, Birmingham B18 7QH

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Left and right sided large bowel cancer

Have significant genetic differences in addition to well known clinical differences

Cancer of the large bowel is the third commonest cancer, and second commonest cause of death due to cancer in the United Kingdom. In 1994, there were 28 904 registered new cases and about 15 740 deaths from colorectal cancer in England and Wales.[1] Differences in clinical presentation and surgical management of right and left sided large bowel cancer are well known. For example, right sided tumours typically present at a more advanced stage with symptoms of weight loss and anaemia, whereas left sided tumours often present with rectal bleeding, change in bowel habit, and tenesmus. However, we are now aware of increasing differences in the molecular pathology of carcinomas depending on their laterality

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within the large bowel. These differences will become more relevant as systemic treatments improve.

The large bowel includes both the colon and the rectum. It is continuous, with no definite point microscopically where colon ends and rectum begins. From an anatomical and surgical point of view, the rectum begins at the peritoneal reflection. Endoscopically, the rectosigmoid junction is often defined as 15 cm from the anal margin. The embryological development of the large bowel begins in the fourth week with folding of the primitive endodermal gut tube producing the foregut, midgut, and hindgut. The midgut eventually develops into distal duodenum, jejunum, ileum, caecum, appendix, ascending colon, and proximal two thirds of the transverse colon. The hindgut develops into the distal third of the transverse colon, the sigmoid colon, rectum, and upper two thirds of the anal canal.

Cancer of the colon and rectum are often combined as colorectal cancer. Both are usually adenocarcinomas with similar histological appearances, arising from normal mucosa of the large bowel.

About 90-95% of cancers of the large bowel are sporadic. Many of these are thought to develop according to the Vogelstein model of carcinogenesis.[2] In this model the transition from normal mucosa to adenoma to carcinoma and metastasis represents sequential defects in genes including adenomatous polyposis coli, k-ras, deleted in colorectal cancer, and p53. However, other mechanisms of carcinogenesis have also been identified, such as gene inactivation by abnormal methylation.[3 4]

Five to 10% of bowel carcinomas are due to inherited conditions including familial adenomatous polyposis and hereditary non-polyposis colorectal cancer. The latter is due to inherited mutations in deoxyribonucleic acid mismatch repair genes such as mutL homolog 1 (hMLH1). Defects in mismatch repair genes lead to variations in the length of microsatellites, known as microsatellite instability.[5] Microsatellites are repetitive deoxyribonucleic acid sequences scattered throughout the genome. About 15% of sporadic colorectal cancers also show microsatellite instability, most often due to inactivation of hMLH1 by methylation.

Microsatellite instability is significantly more common in right sided bowel cancers. One study of 656 patients with Dukes' C carcinoma of colon or rectum showed microsatellite instability in 20% of right sided and 1% of left sided bowel cancers.[6] Inactivation of other genes by methylation, such as p14, p15, p16 and O6-methylguanine-DNA-methyl transferase may also be seen.[4] Specific k-ras mutations may also be more common in proximal tumours.[7] Sporadic right sided colorectal cancers showing microsatellite instability may have lower levels of other factors such as vascular endothelial growth factor,[8] and mutant p53.[9] In contrast, left sided bowel or rectal cancers are more likely to show features including aneuploidy, loss of heterozygosity, overexpression of vascular endothelial growth factor, and mutations in genes from the Vogelstein model including p53.[10] The model of co-segregation of different molecular markers is still in development. For example, methylation of O6-methylguanine-DNA-methyl transferase may be associated with k-ras mutation, p53 mutation,[11] and low level microsatellite instability.[12]

Tumours showing microsatellite instability have an improved prognosis.[13 14] The good prognosis of these predominantly right sided cancers may be offset by the fact that they tend to present at a later stage. Reports from one group have suggested that microsatellite instability predicts a benefit from adjuvant chemotherapy particularly in right sided tumours.[9] However, these were not randomised studies and a number of potential biases could have affected the results. In contrast, the features seen predominantly in left sided cancers such as mutant p53, and overexpression of vascular endothelial growth factor are associated with an adverse prognosis and poor response to fluorouracil based chemotherapy. New targeted treatments, such as antivascular endothelial growth factor antibodies, may be appropriate for these tumours. A further overview of colorectal cancer is awaited to confirm whether cancers of the colon derive more clinical benefit from fluorouracil than rectal cancers. Newer agents such as irinotecan and oxaliplatin may also show differing responses dependent on site of disease or molecular pathology. In the future both the primary site and genetic features of an individual cancer may determine the systemic treatment.

Susan Richman *senior scientific officer*
Julian Adlard *oncology clinical research fellow*

Department of Pathology, Leeds General Infirmary, LS1 3EX

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